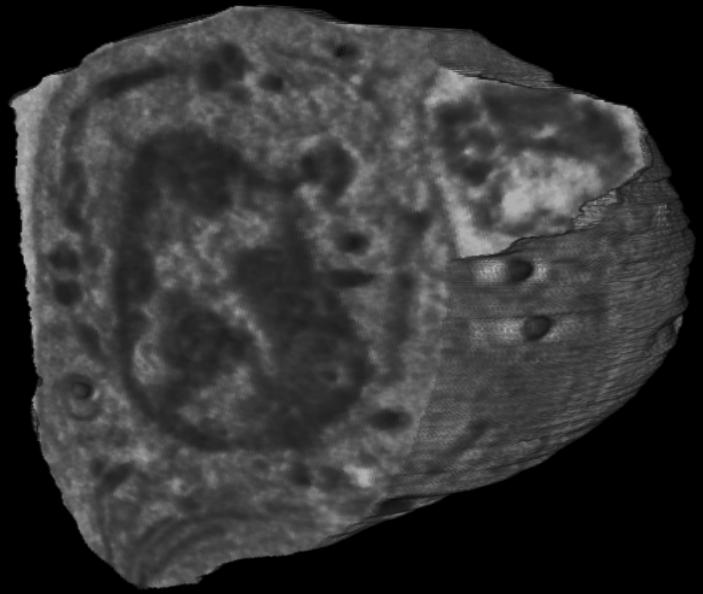
Chromatin Reorganization during Viral Infection



Maija Vihinen-Ranta
University of Jyvaskyla
Finland

Myllys M

Herpes simplex virus type 1 (HSV-1)

Common viral infection

USA 68 %
Finland 52-57 %

Transmitted mainly horizontally in childhood or sexually later

Cold sores and genital herpes

Permanent infection
- Latent or lytic



http://medical-enc.com/herpes_simplex.html

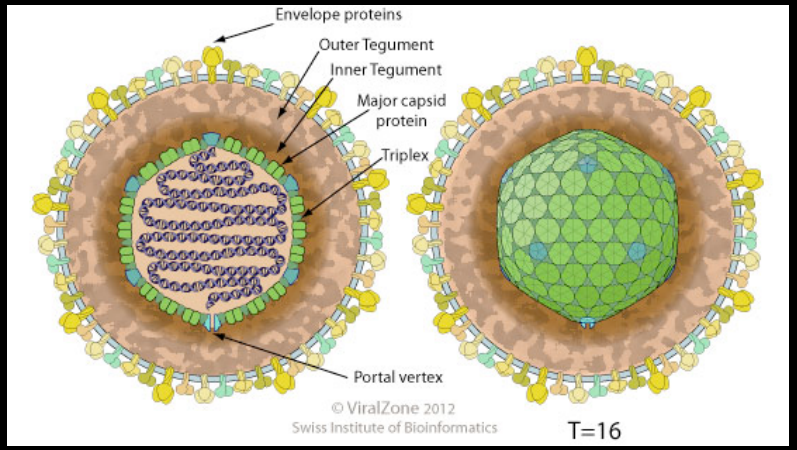
HSV-1

Structure

Large, enveloped icosahedral capsids
Nucleocapsid diameter is 125 nm - with envelope 150-200 nm

Genome

Linear double-stranded DNA genome (152 kb)
Encodes 77 proteins



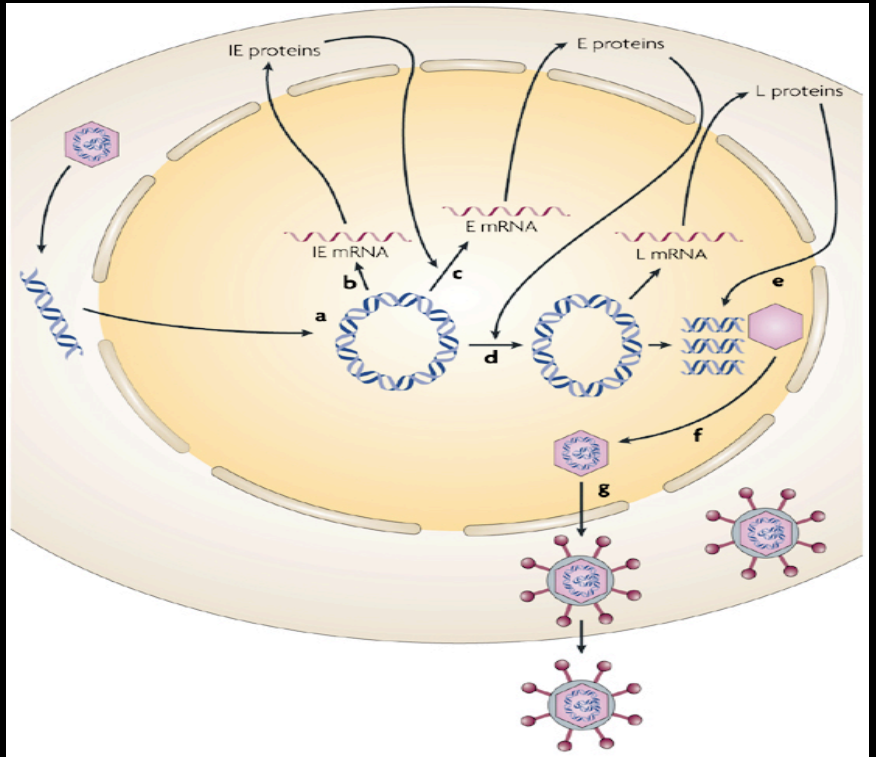
viralzone.expasy.org/all_by_species/178.html

Herpes simplex virus type 1 (HSV-1)

Common viral infection

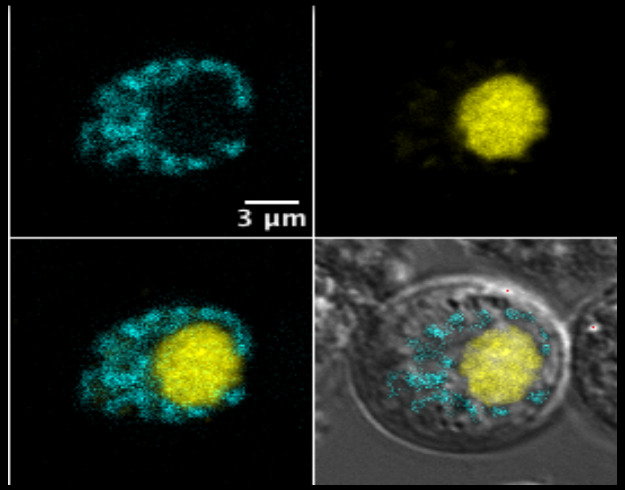
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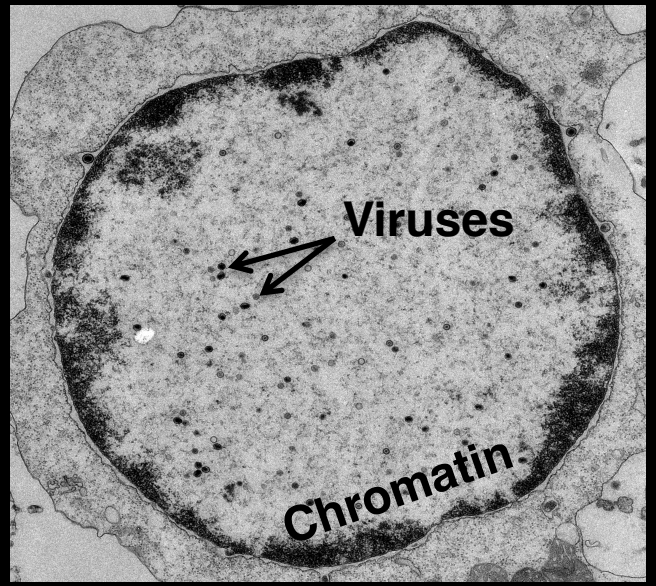
Permanent infection
- Latent or lytic



Knipe & Cliffe (2008).Nature Reviews Microbiology

How does virus reorganize host cell chromatin?





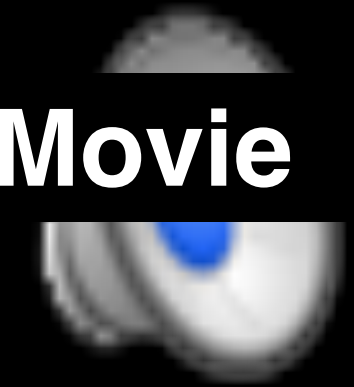
Viral protein (HSV-1 EYFP-ICP4)
Chromatin (ECFP-H2B)

Aho et al. (2017). Sci Rep 16;7:3692.

Soft X ray tomography (SXT) imaging of chromatin

Infected cell

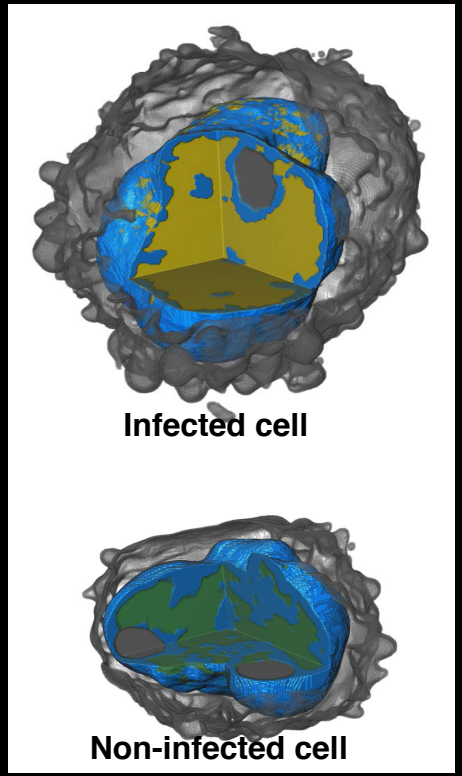
Non-infected cell



Nucleoplasm /VRC)
Euchromatin
Heterochromatin

Linear absorbtion coefficient (LAC) (1/μm)

Virus-induced changes in nucleus and chromatin



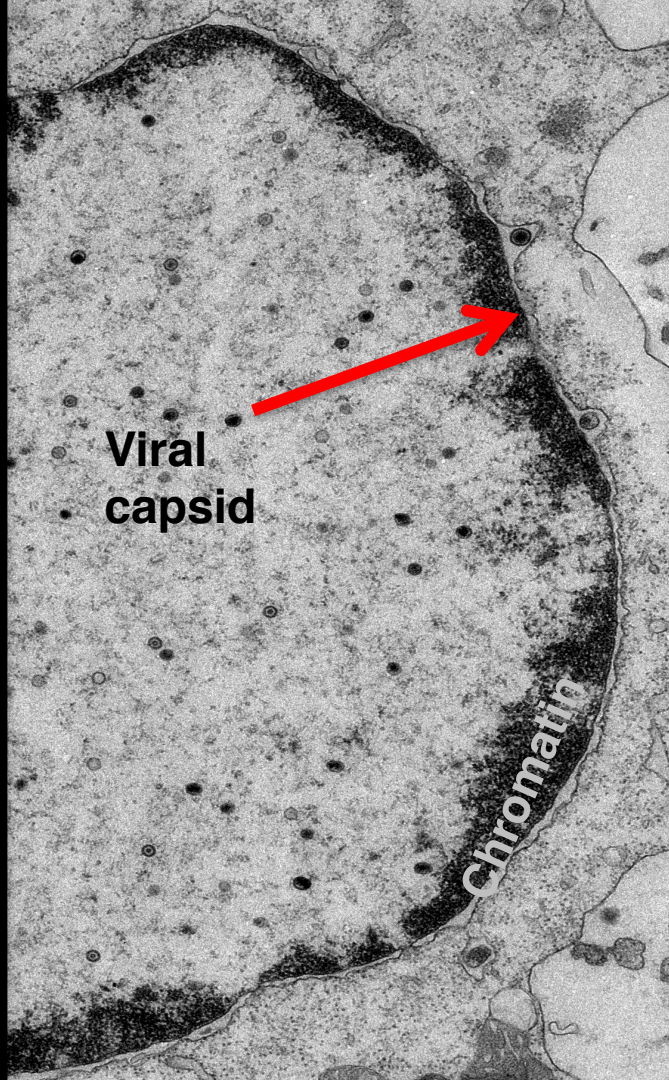
Volume of nucleus and cytoplasm is increased

Majority of chromatin is concentrated in nuclear periphery

Chromatin is more tightly packed in infection

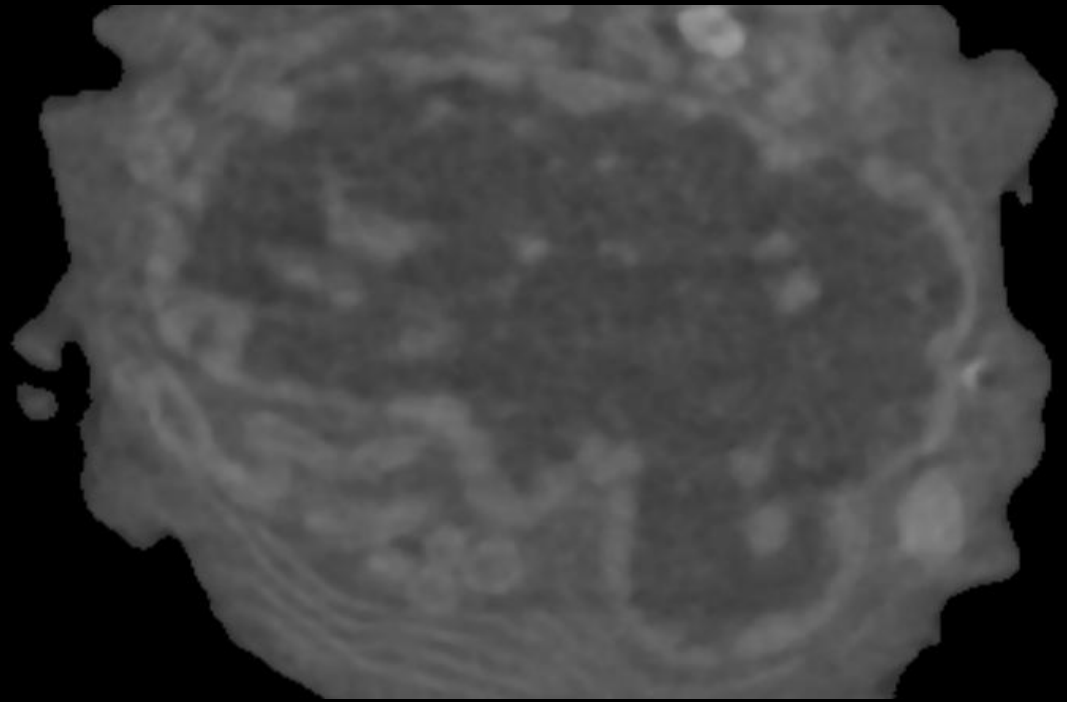
Aho et al. (2017). Sci Rep 16;7:3692

Is nuclear egress of viral capsids limited by peripheral chromatin?



Random walk simulations of capsid nuclear transport

3D reconstruction of nucleus generated from SXT orthoslices



Marginalized chromatin restricts viral capsid diffusion towards the nuclear envelope

Aho et al. (2017). Sci Rep 16;7:3692.
Aho et al. (2016). Phys Rev E 93, 043309.

Channels through chromatin allow passage of capsids

Movie

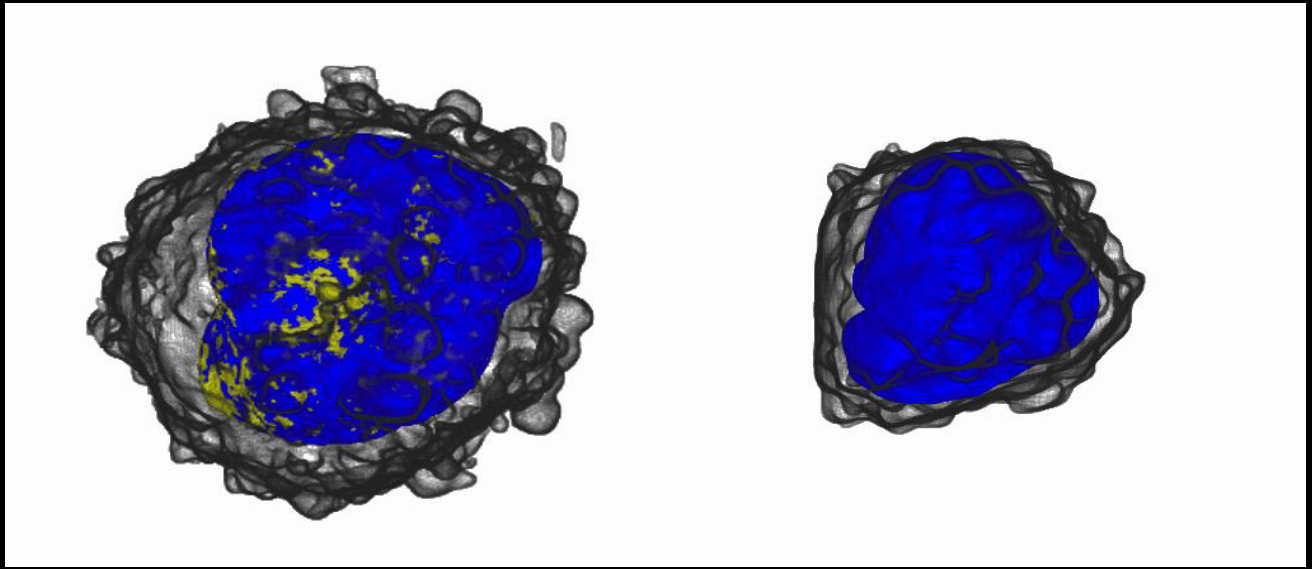
Export locations:
Infected cells: 150 ± 20
Non-infected cells: 37 ± 17

Aho et al. (2017)

Are there low-density areas in compacted chromatin ?

Infected cell

Non-infected cell

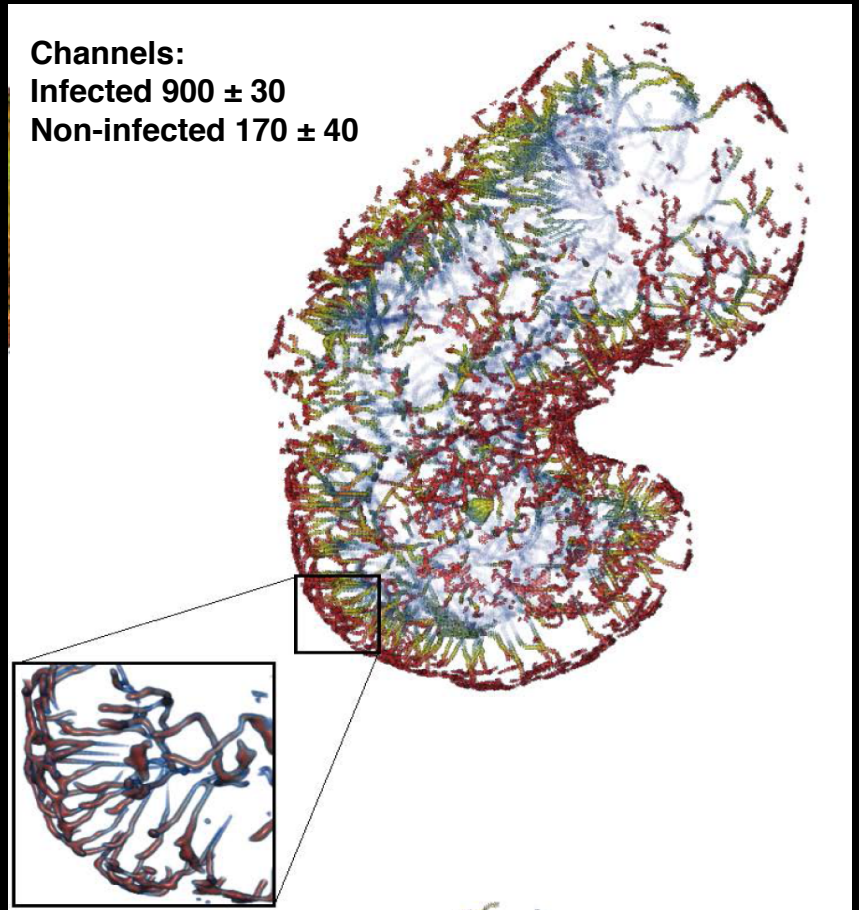


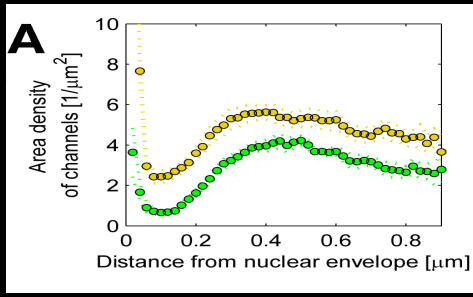
Nucleoplasm with viral replication compartment
Nucleoplasm with euchromatin
Heterochromatin

Myllys et al. (2016). Scientific Reports 6: 28844

Viruses form channels through chromatin

Low LAC areas in the close proximity to nuclear envelope reduced to skeletonized structure

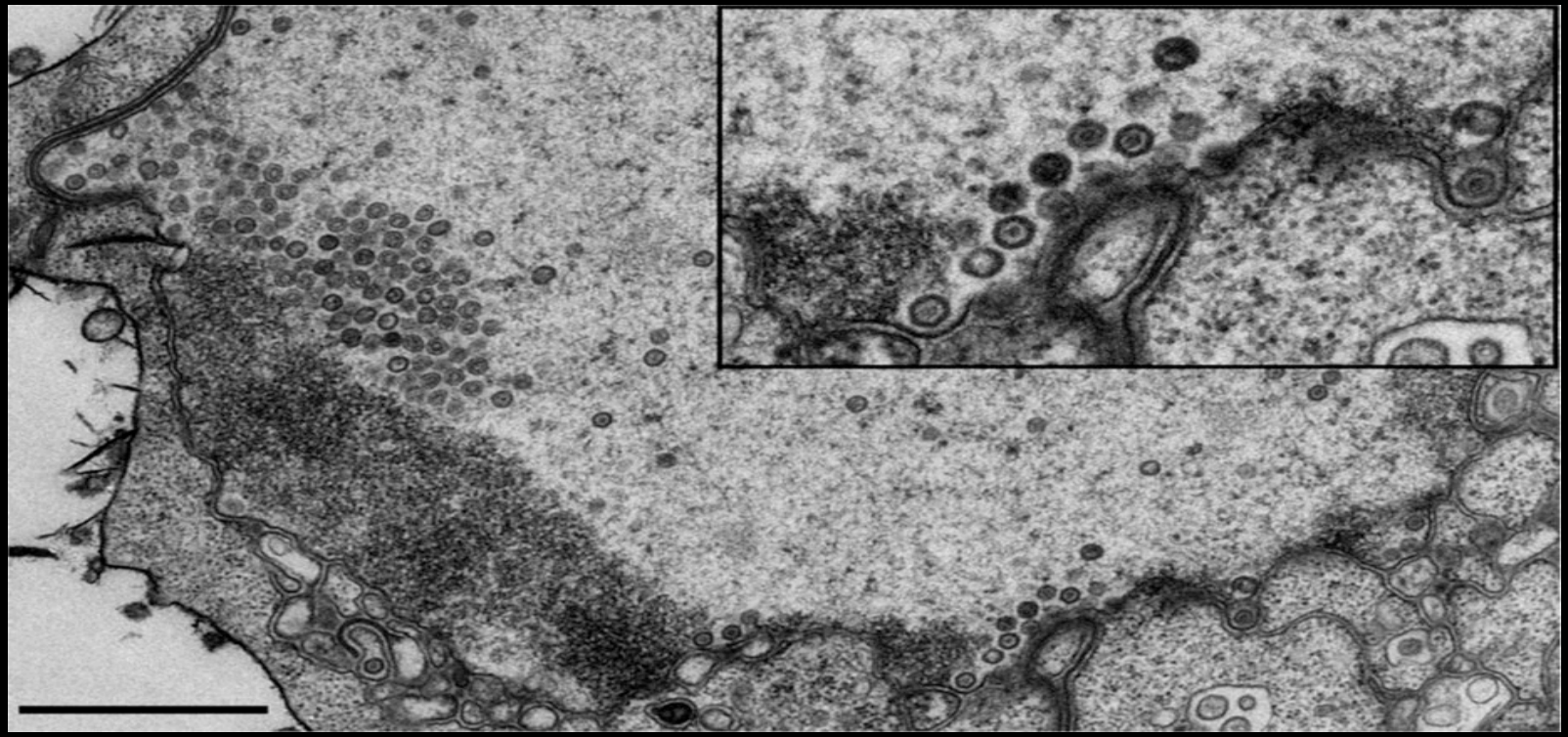




Infected
Non-infected

Myllys et al. (2016)

Capsids in perinuclear low-chromatin regions



Myllys et al (2016)

Conclusions

Formation of HSV-1 replication compartment induces compaction of the host chromatin into nuclear periphery

Channels through compacted chromatin are required for nuclear egress of viral nucleocapsid

Herpesvirus nucleus interactions project

J&AE JANE AND AATOS ERKKO FOUNDATION

2015 – 2018

Maija Vihinen-Ranta and Jussi Timonen

Vesa Aho

Teemu Ihalainen

Thomas Kühn

Elina Mäntylä

Keijo Mattila

Markko Myllys

Satu Hakanen













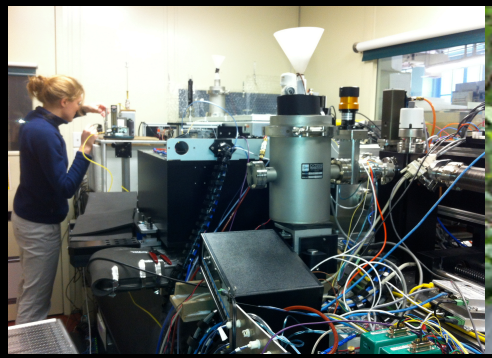


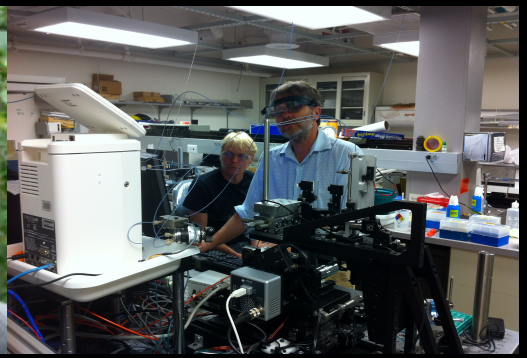




3D Soft x-ray tomography (SXT)

National Center for X-ray Tomography (NCXT)
Lawrence Berkeley National Laboratory (LBNL), Berkeley, CA





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